

PB87-191797

Neurobehavioral Effects of
Environmental Tobacco Smoke

(U.S.) Health Effects Research Lab.
Research Triangle Park, NC

May 87



U.S. Department of Commerce
National Technical Information Service
NTIS

EPA/600/D-87/154
May 1987

NEUROBEHAVIORAL EFFECTS OF ENVIRONMENTAL TOBACCO SMOKE

Vernon A. Benignus

Research Psychologist
United States Environmental Protection Agency
Health Effects Research Laboratory
Neurotoxicology Division
Neurophysiology Branch
Mail Drop 58
Research Triangle Park, NC 27711

and

Research Professor
Dept. of Psychology
University of North Carolina
Chapel Hill

HEALTH EFFECTS RESEARCH LABORATORY
OFFICE OF RESEARCH AND DEVELOPMENT
U.S. ENVIRONMENTAL PROTECTION AGENCY
RESEARCH TRIANGLE PARK, NC 27711

REPRODUCED BY
U.S. DEPARTMENT OF COMMERCE
NATIONAL TECHNICAL
INFORMATION SERVICE
SPRINGFIELD, VA. 22161

TECHNICAL REPORT DATA <i>(Please read Instructions on the reverse before completing)</i>		
1. REPORT NO. EPA/600/D-87/154	2.	3. RECIPIENT'S ACCESSION NO.
4. TITLE AND SUBTITLE Neurobehavioral Effects of Environmental Tobacco Smoke	5. REPORT DATE May 1987	
	6. PERFORMING ORGANIZATION CODE	
7. AUTHOR(S) Benignus, V.A.	8. PERFORMING ORGANIZATION REPORT NO.	
9. PERFORMING ORGANIZATION NAME AND ADDRESS HERL, NTD, NPB, MD58	10. PROGRAM ELEMENT NO.	
	11. CONTRACT/GRANT NO.	
12. SPONSORING AGENCY NAME AND ADDRESS Health Effects Research Laboratory, RTP Office of Research and Development U.S. Environmental Protection Agency Research Triangle Park, NC 27711	13. TYPE OF REPORT AND PERIOD COVERED	
	14. SPONSORING AGENCY CODE EPA/600/11	
15. SUPPLEMENTARY NOTES		
16. ABSTRACT Effects of environmental tobacco smoke on neurobehavioral variables has not received much research attention. In order to try to predict effects of environmental tobacco smoke, neurobehavioral effects of mainstream smoke were reviewed and, in conjunction with what is known about body uptake of components of environmental tobacco smoke, conjectures were made about the probable effect of environmental tobacco smoke. Effects of mainstream smoke differ in smokers and nonsmokers. Mainstream smoke has a beneficial effect on vigilance in habitual smokers. The effect in nonsmokers is, however, less clear and may be disruptive. In both smokers and nonsmokers, however, mainstream smoke produces increased tremor and reduced fine motor skills. The neurobehaviorally active substances in mainstream smoke appear to be nicotine and carbon monoxide. There is evidence of reversing effects over a period of time following the exposure to mainstream smoke which may be due to either pharmacokinetic events or to less well specified rebound phenomena. Nicotine levels in the blood of nonsmokers exposed to environmental tobacco smoke rarely rises above the level of 6% of that of the smokers in the same space. The COHb of nonsmokers exposed to environmental tobacco smoke sometimes approaches that of the smokers in the same space. It appears that COHb is the more important consequence of environmental tobacco smoke for neurobehavioral effects, since nicotine levels in nonsmokers only reach a small fraction of those in smokers.		
17. KEY WORDS AND DOCUMENT ANALYSIS		
a. DESCRIPTORS	b. IDENTIFIERS/OPEN ENDED TERMS	c. COSATI Field/Group
18. DISTRIBUTION STATEMENT RELEASE TO PUBLIC	19. SECURITY CLASS (This Report) UNCLASSIFIED	21. NO. OF PAGES 27
	20. SECURITY CLASS (This page) UNCLASSIFIED	22. PRICE

NOTICE

This document has been reviewed in accordance with U.S. Environmental Protection Agency policy and approved for publication. Mention of trade names or commercial products does not constitute endorsement or recommendation for use.

ABSTRACT

Effects of environmental tobacco smoke on neurobehavioral variables has not received much research attention. In order to try to predict effects of environmental tobacco smoke, neurobehavioral effects of mainstream smoke were reviewed and, in conjunction with what is known about body uptake of components of environmental tobacco smoke, conjectures were made about the probable effect of environmental tobacco smoke.

Effects of mainstream smoke differ in smokers and nonsmokers. Mainstream smoke has a beneficial effect on vigilance in habitual smokers. The effect in nonsmokers is, however, less clear and may be disruptive. In both smokers and nonsmokers, however, mainstream smoke produces increased tremor and reduced fine motor skills. The neurobehaviorally active substances in mainstream smoke appear to be nicotine and carbon monoxide. There is evidence of reversing effects over a period of time following the exposure to mainstream smoke which may be due to either pharmacokinetic events or to less well specified rebound phenomena.

Nicotine levels in the blood of nonsmokers exposed to environmental tobacco smoke rarely rises above the level of 6% of that of the smokers in the same space. The COHb of nonsmokers exposed to environmental tobacco smoke sometimes approaches that of the smokers in the same space. It appears that COHb is the more important consequence of environmental tobacco smoke for neurobehavioral effects, since nicotine levels in nonsmokers only reach a small fraction of those in smokers.

TABLE OF CONTENTS

I.	INTRODUCTION.....	3
II.	EFFECTS OF MAINSTREAM SMOKE.....	4
	A. Methodological.....	4
	B. Beneficial Effects of Mainstream Smoke.....	7
	C. Deleterious Effects of Mainstream Smoke.....	8
	D. Conclusions About Mainstream Smoke.....	10
III.	COMBINED EFFECTS OF MAINSTREAM SMOKE AND OTHER SUBSTANCES..	12
	A. Drugs and Mainstream Smoke.....	12
	B. CO and Mainstream Smoke.....	13
IV.	EFFECTS OF ENVIRONMENTAL TOBACCO SMOKE.....	13
	A. Measures of exposure.....	14
	1. Concentrations in Environment.....	14
	2. Body Burdens.....	15
	3. Conclusions-Environmental Tobacco Smoke Exposures.....	16
	B. Neurobehavioral Effects of Environmental Tobacco Smoke.....	16
V.	EFFECTS OF ENVIRONMENTAL TOBACCO SMOKE IN COMPRESSED AIR UP TO FIVE ATMOSPHERES.....	17
VI.	SUMMARY AND CONCLUSIONS.....	18
VII.	REFERENCES.....	21

NEUROBEHAVIORAL EFFECTS OF ENVIRONMENTAL TOBACCO SMOKE

Vernon A. Benignus

It is well known that long term exposure to tobacco smoke has deleterious effects on pulmonary and cardiovascular health (National Research Council, 1986). It is possible that the acute neurobehavioral effects of tobacco smoke exposure may lead to consequences in terms of health and safety which are of equal or greater importance than the effects of chronic exposure. A short term decrement in performance of a critical task by a person exposed to tobacco smoke could produce accidents or consequences affecting many persons other than the exposed person.

Effects of environmental tobacco smoke on neural and behavioral variables have not been studied except for sensory measures such as odor and irritation. An important body of literature does, however, exist in the area of the neurobehavioral effects of smoking in smokers themselves, i.e., on the effects of mainstream smoke. The present paper a) reviews and summarizes the effects of mainstream smoke on neurobehavioral variables, b) offers speculations about the effects of mainstream smoke in combination with other pollutants, e.g., carbon monoxide (CO) and solvents and c) attempts to generalize the effects of mainstream smoke to those of environmental tobacco smoke at one and five atmospheres. The latter generalization is not without hazard, but, in view of the lack of data on environmental tobacco smoke, little better can be

offered.

Among the ca. 3800 compounds identified in tobacco smoke (National Research Council, 1986), few are present in sufficient quantities to rank as important contributors to acute neurobehavioral effects. The two outstanding substances are carbon monoxide and nicotine. While other substances are present they are unlikely candidates for one reason or another. Carbon dioxide, for instance, exceeds the concentration of CO in mainstream smoke, but, is not important to behavioral variables in the observed concentrations. As a provisional procedure, it will be assumed that CO and nicotine are the substances of concern.

EFFECTS OF MAINSTREAM SMOKE

Methodological.

One of the inherent problems in research on the neurobehavioral effects of tobacco smoking is that of providing an adequate blind control for the smoking condition in an experiment. The problem was first addressed in a partially adequate way by Clark Hull (1924) who used a heated, humidified, sham-smoking device. Subsequently, frequently used control conditions were puffing on unlit cigarettes or smoking non-tobacco cigarettes. A somewhat more adequate procedure has been to use cigarettes of different "strength" ranging from no nicotine to high nicotine. The latter technique controls only for nicotine, not for other possibly neurobehaviorally active ingredients of smoke, e.g. CO. In any of the above methods it is questionable to assume that the subject is blind since at least nicotine has interoceptive effects. It therefore appears that

the problem of experimental control for the smoking condition in an experiment has not been adequately solved and may not be easily soluble.

Another of the inherent problems in smoking studies is the administration of the "dose" of smoking. There are many variables about the style of smoking which determine the dose of mainstream smoke received, e.g., degree of inhalation, duration of smoke retention and rate of burning of smoking material. It appears that there is much variation across habitual smokers and across time or situation within individual smokers in these patterns. Solutions to the problems of dose control involve compromises between the extremes of artificial dosing to ad lib intake. The former offers good experimental control but nonrepresentative design while the latter extreme offers the inverse. Again no clear solution is readily apparent even though several strategies are available. The problem of dose in environmental tobacco smoke is further complicated by such variables as living space volume and ventilation, the numbers of smokers and their spatial distributions. An excellent summary of dose parameters for both mainstream smoke and environmental tobacco smoke is to be found in National Research Council (1986).

As is true of any habitual drug use, there is a problem in the separation of acute and chronic effects in habitual smokers. Certainly the two are confounded in any condition in which habitual smokers are placed into a smoking condition of an experiment. Chronic effects could be isolated by studying ex-smokers in a non-smoking condition. Temporarily abstaining

smokers, however, might exhibit withdrawal symptoms which would introduce new problems. The nicotine metabolism of habitual smokers is also more rapid due to enzyme induction (National Research Council, 1986)

Another experimental control problem is related to both the problems of dose control and the confounding of chronic and acute effects. This is the problem of recent and distant history of smoking in the individual. If chronic effects are large, it becomes important to know the cumulative dose (or some other relevant parameter) of smoking for each subject. No good measure of such exists (Henningfield, 1984). If recent history is important then one must control not only the subject's smoking during a smoking condition but during the hours or days just before the experiment. Fortunately, measures of recent smoking history are available (Henningfield, 1984).

Another experimental control problem concerns the matching of habitual smokers with nonsmokers on relevant parameters or at least assuring that no bias exists between groups. It is quite likely that habitual smokers differ from non-smokers on such matters as health concerns, response to peer pressure, ability to delay gratification and "addictability" to list but a few possibilities (Hull, 1924). Any experimental contrasts involving habitual smokers vs. nonsmokers are likely to be confounded with variables related to subject characteristics.

Researchers in the area of smoking research have not always attended to all or even many of the above methodological problems. In addition to such experimental control problems as those cited above, many studies have been poorly conceived,

designed or analyzed. The frequent use of anti-conservative statistical analyses (Muller, Barton and Benignus, 1984) has probably contributed a number of type I errors (deciding that an effect was significant when in the population no effect existed). Both lack of experimental control and anti-conservative statistics might well be the source of controversy about most neurobehavioral effects of smoking. Fortunately, there are a few neurobehavioral effects attributable to smoking which have been reported often enough to make them believable even if some confounding with other variables cannot be excluded.

Beneficial Effects of Mainstream Smoke.

Smoking of tobacco appears to be beneficial to the performance of tasks which involve vigilance, i.e. long duration, uninterrupted but non-demanding work. Such results were reported by Hull (1924), Tarriere and Hartman (1964), Heimstra, Bancroft and Dekock (1967), Frankenhaeuser, et al. (1971), Myrsten, et al. (1972), Wesnes and Warburton (1983b), Wesnes, Warburton and Matz (1983), Tong, Henderson and Chippenfield (1980) and Williams (1980). In general, the vigilance performance of habitual smokers in the smoking condition declined least as a function of time, habitual smokers in the nonsmoking condition declined most and nonsmokers (when included) were between. Apparently, habitual smokers benefit from smoking in a vigilance situation with respect to nonsmokers. When differing strengths of cigarettes were used, results were ordinal in dose. Use of nicotine tablets instead of smoking duplicated the effects in smokers but disrupted performance in nonsmokers (Wesnes and

Warburton, 1978, 1983). Other studies did not show such clear effects but were also flawed in important ways (Ashton, et al., 1972, Mangan, 1982).

The vigilance improvement seems to occur to a greater extent in smokers who rate high on the Eysenck and Eysenck (1964) neuroticism scale but to a lesser degree (if at all) in low neuroticism subjects (Warburton and Wesnes, 1978). Neurobehavioral effects may also depend upon the arousal level of the smoker and the arousing nature of the task (Myrsten, et al., 1975).

As tasks become more complex but remain long in duration and uninterrupted, results become less consistent. Hull (1927) reported that smoking produced increased reading speed but slower mental arithmetic performance with increased errors. Friedman (1972) partially replicated Hull's findings in that she reported increased mental arithmetic speed but increased errors due to smoking. Other literature (beyond the scope of this review) appear to show progressively less consistent results as tasks become less vigilance-like.

Deleterious Effects of Mainstream Smoke.

In all cases in which motor tremor was studied, tobacco smoking increased such tremor. Hull (1924) reported increased tremor, heart rate and blood pressure after pipe smoking as compared to control conditions of sham smoking heated humidified air. Habitual smokers had greater effects than nonsmokers. Highly similar results, although sometimes not as well controlled, were reported by others (Edwards, 1948; Frankenhaeuser, et al. 1968; Frankenhaeuser, Myrsten and Post,

1970; Smith, Tong and Leigh, 1977; Lippold, Williams and Wilson, 1980; Shiffman, et al. 1983). That habitual smokers showed a more dramatic increase in tremor may reflect possibly higher resting levels of nicotine.

Most of the increased tremor in the above articles was measured in simple stylus-in-hole tests or by transducers attached to extremities which subjects attempted to hold steady. It is not clear how such increased tremor might generalize to more "real world" tasks such as small parts manipulation or hand-eye coordination. A tracking measure as part of a driving simulator showed that nonsmokers performed best, habitual smokers in the smoking condition were worse and deprived smokers had the largest tracking error (Heimstra, Bancroft and Dekock, 1967) although the measure of tracking error did not lend itself to determining what aspects of tracking accounted for the difference. It is possible that motor tremor was the important variable. No other less abstract test of motor skills and smoking was found.

Simple reaction time has been reported to be decreased by smoking in habitual smokers (Heimstra, Bancroft and Dekock, 1967; Smith, Tong and Leigh, 1977; Wesnes and Warburton, 1983a, 1984). Comparison of habitual smokers with nonsmokers (Heimstra, Bancroft and Dekock, 1967) indicated that habitual smokers in the smoking condition had the shortest reaction time, deprived habitual smokers the longest and nonsmokers fell between. Cotten, Thomas and Stewart (1971), studying habitual smokers reported that while the effects of smoking on simple reaction

time was a decrease during the first five minutes after smoking, a rebound occurred during which simple reaction time was longer than presmoking for about 20-60 minutes. Thus the decrease of reaction time after smoking was not a simple monotone effect but a complex time trend involving both improvement and worsening. It is possible that the early shortening of reaction time was primarily a nicotine effect while the later increased reaction time was due to COHb effects after nicotine had been eliminated. It is also possible that a post-nicotine rebound effect might have occurred. Domino (1973) reported a dose-related decreased amplitude of patellar reflex in persons with varied smoking histories immediately after smoking. Reaction times were not reported.

Complex reaction times showed less consistent results. Lyon, et al. (1975) reported that choice reaction time was shortest in nonsmokers, longest in deprived habitual smokers and that smoking in habitual smokers decreased the reaction time but not to as short a value as nonsmokers. Knott (1978 a,b) measured simple reaction time in habitual smokers with distracting noise. Only deprived habitual smokers had longer reaction times with respect to the no-noise condition. While it appears that smoking tends to first decrease and then increase simple reaction time, trends are not known for complex reaction times. The biggest effect in reaction time appears to be on the deprived habitual smoker.

Conclusions About Mainstream Smoke.

Tobacco smoking and its effects on military task performance was recently reviewed in an extensive manner (Dyer, 1986).

Other, less extensive reviews of neurobehavioral effects exist (Thornton, 1978; Emley and Hutchinson, 1984; Wesnes and Warburton, 1983b; Henningfield, 1984). From these reviews and from the wider literature above the following conclusions may be drawn.

- I. Methodological. Research on neurobehavioral effects of tobacco smoking has a number of inherent problems with experimental control. Experiments are not always well-conceived, designed or executed.
- II. Mixed Effects. Acute neurobehavioral effects of smoking are not always deleterious. Some behaviors are acutely improved by smoking. For many behaviors there is poor agreement among researchers on the effects. Effects may be mitigated by (a) situations (b) smoking style and (c) personality.
 - a. Beneficial Effects. One of the most consistently reported beneficial effects of smoking is improved vigilance performance and related tasks.
 - b. Deleterious Effect. The most consistently reported deleterious effect of smoking is increased motor tremor. Thus tasks requiring precision movements are expected to be impaired.

Too little attention has been paid to the correlation of pharmacological events due to smoking with the measured neurobehavior. Nicotine and COHb are both increased by smoking, but nicotine level falls more rapidly than COHb (Henningfield, 1984; Benowitz, et al. 1982; Coburn, Forster and Kane, 1965).

Thus there may be time related trends explainable by pharmacological events.

COMBINED EFFECTS OF MAINSTREAM SMOKE AND OTHER SUBSTANCES

The combined effects of smoking and any other substance exposure on neurobehavioral variables is only rarely reported. The combined effects of smoking and exposure to other substance will be reviewed. Using what is known about interactions of mainstream smoke with e.g. drugs, generalizations can be made to environmental pollutants.

Drugs and Mainstream Smoke.

Smith, Tong and Leigh (1977) studied the separate and combined effects of smoking and caffeine administration in habitual smokers. The dependent variables were hand steadiness, reaction time and heart rate. Tremor was increased by both smoking and caffeine and their combined effect was additive. Reaction time was decreased by both and effects were additive. Heart rate was increased by both caffeine and smoking individually, but in combination there was no change from baseline. The latter (if replicable) is a prime example of "paradoxical", or non-predictable effects of combination of substances.

Separate and combined effects of smoking and ethanol administration on vigilance were studied by Tong, Henderson and Chippenfield (1980) in habitual smokers. Smoking, with and without ethanol, served to eliminate declining performance over time. Ethanol simply produced an overall decrement in performance during either smoking or abstinence which was not time related. Again, effects were additive (combined linearly

and subtractively as opposed to interactively).

Tong, et al. (1974) studied the separate and combined effects of smoking and ethanol on two-flash thresholds (ability to temporally discriminate two light flashes). Smoking improved performance while ethanol impaired it. When combined, the effects canceled. Again, effects were additive.

CO and Mainstream Smoke.

Since tobacco smoking produces both nicotine and COHb buildup in the body it would appear that CO exposure might exacerbate effects due to COHb from smoking. This might not be true if smokers have adapted to chronic COHb conditions, or, alternatively might be especially true if smokers have been damaged by COHb conditions from smoking. Nicotine and COHb effects might serve to cancel each other since one is a "stimulant" and the other a "depressant". This might not be true in "paradoxical" drug effects which are commonly reported. It is also true that nicotine builds up and is eliminated more rapidly than is COHb so that the early effect of combined exposure might be subtractive while later effects might be depressant.

With little data and much conjecture, it appears that smoking and CO exposure should have important combined effects depending upon the time after administration of CO and the smoking pattern. If such effects occur, then a large segment of the population are at special risk to CO exposure. It is important that such neurobehavioral effects be well understood.

EFFECTS OF ENVIRONMENTAL TOBACCO SMOKE

No studies on the neurobehavioral effects of environmental

tobacco smoke were found (other than those related to odor or irritation). Speculations about such effects in the following are based upon generalizations from environmental tobacco smoke measures and observations of body burdens of smoking products in nonsmokers. Such values can be compared to those of active smokers and the effects of mainstream smoke can be generalized to the effects of environmental tobacco smoke. Such generalization is hazardous at best. Rates of uptake differ as well as peak values. Methodical use of smoking by the smoker, for whatever purpose, is different from the nonsmoker. The method of intake also differs. Other differences can be imagined. Nonetheless, no better procedure than such generalization is available in the absence of research.

Measures of Exposure.

Concentrations in Environment. Rate of production of CO in environmental air is determined by a number of factors (National Research Council, 1986). If the tobacco is allowed to smolder instead of being actively smoked, more CO is produced. The preparation of the tobacco for smoking (cigarettes, cigars, pipe) is also a factor. Even within the class of cigarettes, differences of CO production exist, depending upon the type (nonfilter, filter or perforated filter). The rate of air flow over smoldering tobacco also varies the CO production as would the oxygen content of the air. Finally, the volume and exchange rate of the air into which a fixed amount of CO is mixed also determines CO concentration in the environmental air.

Nicotine production by burning tobacco is determined by similar considerations as those cited for CO (National Research Council, 1986). The problem of estimation of nicotine content of

environmental tobacco smoke is complicated, however, by additional physical considerations. Nicotine in environmental tobacco smoke is almost entirely in the vapor phase (Eudy et al., 1985), but, little is known about its fate.

Body Burdens. For purposes of assessment of effects the environmental concentration is of less importance than the measured body burden of CO and nicotine. For CO effects, the relevant variable is usually taken to be the level of carboxyhemoglobin (COHb) as discussed by Coburn (1979) since this variable is related to oxygen delivery. For nicotine, the relevant variable is the nicotine blood level since the presence of nicotine in the blood is a stimulant.

As would be expected from the discussion of the variables controlling the environmental air concentrations of CO and nicotine, the same factors determine body burdens. Therefore, it is not possible to cite a single ratio of COHb or blood nicotine level in smokers to nonsmokers. Ranges abstracted from various studies must suffice.

Mean levels of COHb in cigarette smokers were 4.7% (Wald et al., 1981, 1984). Exposure to environmental tobacco smoke has been reported to produce no elevation of COHb of nonsmoking attendants over baseline measures in airline cabin smoking sections (Folliart et al., 1983). In the other extreme, nonsmokers sharing an unventilated room with smokers had a COHb increase comparable to that of a smoker who had just consumed one cigarette (Jarvis et al., 1983). Unless specific conditions are known or in situ measures of COHb are made, the importance of

environmental tobacco smoke to neurobehavior is not estimable.

Since nicotine is present in the blood only due to environmental exposure, any nicotine blood level in non-tobacco users is usually due to environmental tobacco smoke. In most studies of nicotine blood levels of nonsmokers (National Research Council, 1986), the values were only a few percent of that of the nonsmokers. It is noteworthy that in flight attendants studied by Folliart, et al. (1983), whose COHb had not been elevated by environmental tobacco smoke, the nicotine level was about doubled. Even in the worst reported case (Hoffmann et al., 1984), nicotine levels were no more than 6% of those of smokers.

Conclusions-Environmental Tobacco Smoke Exposures. Level of COHb in nonsmokers exposed to environmental tobacco smoke was shown to be more variable and dependent upon exposure conditions than was nicotine level. Nicotine levels, even in worst reported cases, never reached more than 6% of that observed in active smokers. The level of COHb in nonsmokers, however, approached that of active smokers in worst case conditions. It is not clear why these differences should occur, but, there are important and large differences in the uptake and elimination rates of the two substances. It may be tentatively concluded that, when environmental tobacco smoke becomes neurobehaviorally important, it is the COHb which is the variable of concern for the nonsmokers.

Neurobehavioral Effects of Environmental Tobacco Smoke

If the above conjecture about the importance of COHb in consideration of the effects of environmental tobacco smoke is true, then further speculation about behavioral effects is simplified. While active smokers achieve high levels of both

COHb and nicotine, nonsmokers exposed to environmental tobacco smoke have mainly elevated COHb. The neurobehavioral effects of environmental tobacco smoke in nonsmokers should therefore be similar to those of CO exposure.

EFFECTS OF ENVIRONMENTAL TOBACCO SMOKE IN COMPRESSED

AIR UP TO FIVE ATMOSPHERES

Extension of conjectures about neurobehavioral effects of environmental tobacco smoke into the area of increased atmospheric pressure concomitantly extends the hazard of conjectural error. If, however, CO is the substance of primary concern at one atm, then it might also be so at five atm. It has been estimated by use of mathematical models (see previous chapter) that COHb formation is accelerated by elevated pressure but that the same asymptotic level is approached as at one atm. Since COHb formation is slow, this means that for short exposures, the asymptote is not approximated. At elevated pressure, then, a higher COHb level should occur for a fixed, short, exposure. The effects of environmental CO not due to environmental tobacco smoke would be simply additive.

Quantitative information on the rate of or, asymptotic value of nicotine uptake at elevated atmospheric pressure, was not available to this reviewer. It is probable that the rate of uptake will be increased. For short exposures, therefore, the maximum value of body burden could also be increased at elevated pressure. Supposing that the nicotine level in blood were to be increased by a unit factor of pressure, the nicotine level due to the worst case of environmental tobacco smoke would not exceed

30% of that reached by the smoker in the same atmosphere. Depending upon the environmental levels, this amount of nicotine could become behaviorally important.

The relative importance of CO and nicotine in compressed air containing environmental tobacco smoke would seem to depend upon the relative levels of the two compounds in the atmosphere. Since the amount of COHb in nonsmokers due to environmental tobacco smoke is highly variable, the nicotine component could become more important at pressure. Without more data on (a) the environmental levels in question and (b) the relative uptake of nicotine at elevated atmospheric pressure, the question of relative importance of the two components must remain unanswered.

SUMMARY AND CONCLUSIONS

The effects of environmental tobacco smoke on neural and behavioral variables has not received much research attention. In order to try to predict the effects of environmental tobacco smoke, the fairly well known neurobehavioral effects of mainstream smoke were reviewed and, in conjunction with what is known about body uptake of the components of environmental tobacco smoke, conjectures were made about the probable effects of environmental tobacco smoke. From a sparse literature of the combined effects of mainstream smoke and other neurobehaviorally active substances, an attempt was made to predict which substances would interact in important ways. Finally, an effort was made to generalize the conjectures to hyperbaric conditions about which no data were found.

Clearly this paper contains conjectural material, in some cases of the third order. Such speculation is, at best,

hazardous. In the absence of data, however, little else can be done. The reader should be aware of the nature of the conclusions and should place appropriate weight upon them. Perhaps the major function of this review and conclusions will be to point up the ignorance in this area and to help generate hypotheses for testing.

Neurobehavioral Effects of Mainstream Smoke.

The effects of mainstream smoke differ in smokers and nonsmokers. Mainstream smoke has a clearly beneficial effect on vigilance in habitual smokers. The effect in nonsmokers is, however, less clear and may even be disruptive. In both smokers and nonsmokers, however, mainstream smoke produces increased tremor and therefore reduced fine motor skills. The neurobehaviorally active substances in mainstream smoke appear to be nicotine and carbon monoxide.

There is evidence of reversing effects over a period of time following the exposure to mainstream smoke which may be due to either pharmacokinetic events or to less well specified rebound phenomena. Situational variables, personality and reason for smoking may be important modifiers of effects. There is evidence that, at least for the short term effects, substances such as ethanol and caffeine have additive effects to those of mainstream smoke although the effects are occasionally anomalous.

Effects of Environmental Tobacco Smoke.

Uptake of Environmental Tobacco Smoke. Nicotine levels in the blood of nonsmokers exposed to environmental tobacco smoke rarely rises above the level of 6% of that of the smokers in the

same space. The COHb of nonsmokers exposed to environmental tobacco smoke is sometimes quite low, approaching endogenous levels, while in other cases the COHb of the nonsmoker approaches that of the smokers in the same space. The variables which determine the uptake of CO are probably ventilation and smoking style of the smokers. The half life of COHb is longer than that of nicotine thus producing more accumulation over repeated exposures than would be expected for nicotine. It appears that COHb is the more important consequence of environmental tobacco smoke for neurobehavioral effects, since nicotine levels in nonsmokers only reach a small fraction of those in smokers.

Conjectures. Since COHb formation appears to be the pollutant of neurobehavioral concern in environmental tobacco smoke, it seems reasonable to predict that the effects of environmental tobacco smoke would be the same as those of CO exposure in general. It would also seem that the effects of environmental CO not due to environmental tobacco smoke would be additive to effects of CO from environmental tobacco smoke. In hyperbaric situations the effect of environmental tobacco smoke should seem to be the same as that of CO at similar pressures. In the latter case, COHb appears to form more rapidly and thus for short exposures to CO, more COHb would form.

The main burden of this paper is that there are logical reasons to believe that an acute neurobehavioral effect may occur due to environmental tobacco smoke. Environmental tobacco smoke is a potentially important co-pollutant with other sources of CO. Research on this topic is needed if more than conjecture is required.

- Ashton, H., Savage, R.D., Telford, R., Thompson, J.W., and Watson, D.W. "The effects of cigarette smoking on the response to stress in a driving simulator." British Journal of Pharmacology. (1972) 45:546-556.
- Benowitz, N.L., Kuyt, F., and Jacob, P. "Circadian blood nicotine concentrations during cigarette smoking." Clinical Pharmacology and Therapy. (1982) 32:758-764.
- Coburn, R.F., Forster, R.E., and Kane, P.B. "Considerations on the physiological variables that determine the blood carboxyhemoglobin concentrations in man." Journal of Clinical Investigation. (1965) 44:1899-1910.
- Coburn, R.F. "Mechanisms of carbon monoxide toxicity." Preventive Medicine. (1979) 8:310-322.
- Cotten, D.J., Thomas, J.R., and Stewart, D. "Immediate effects of cigarette smoking on simple reaction time of college male smokers." Perceptual and Motor Skills. (1971) 33:336.
- Domino, E.F. "Neuropsychopharmacology of nicotine and tobacco smoking." IN: Smoking Behavior: Motives and Incentives. W.L. Dunn Jr. (eds). John Wiley & Sons, Washington DC. (1973) p 5-31.
- Dyer, F.N. Smoking and Soldier Performance (Final Report). U.S. Army Aeromedical Research Laboratory, Fort Rucker, Alabama. (1986)
- Edwards, A.S. "The effect of smoking on tremor." Journal of Applied Psychology. (1948) 32:150-158.
- Emley, G.S., and Hutchinson, R.R. "Behavioral effects of nicotine." IN: Advances in Behavioral Pharmacology. T. Thompson, P.B. Dews, and J.E. Barrett (eds). Academic Press, Inc., Orlando. (1984) vol 4, p 105-129.
- Eudy, L.W., Thome, F.A., Heavner, D.L., Green, C.R., and Ingebrethsen, B.J. Studies on the vapor-particulate phase distribution on environmental nicotine by selected trapping and detection methods. Presented at 39th Tobacco Chemists' Research Conference, Montreal Canada. (1985)
- Eysenck, H.J., and Eysenck, S.B.G. Manual of the Eysenck Personality Inventory. University of London Press, London. (1964)
- Folliart, D., Benowitz, N.L., and Becker, C.E. "Passive absorption of nicotine in airline flight attendants." New England Journal of Medicine. (1983) 308:1105.
- Frankenhaeuser, M., Myrsten, A.L., Waszak, M., Neri, A., and Post, B. "Dosage and time effects of cigarette smoking." Psychopharmacologia (Berl). (1968) 13:311-319.

- Frankenhaeuser, M., Myrsten, A.L., and Post, B. "Psychophysiological reactions to cigarette smoking." Scandinavian Journal of Psychology. (1970) 11(4):237-245.
- Frankenhaeuser, M., Myrsten, A.L., Post, B., and Johansson, B. "Behavioural and physiological effects of cigarette smoking in a monotonous situation." Psychopharmacologia (Berl). (1971) 22:1-7.
- Friedman, L.N. "The effects of smoking upon the performance of mental tasks of light and heavy smokers." Dissertation Abstracts International. (1972) 33(6):1.
- Heimstra, N.W., Bancroft, N.R., and DeKock, A.R. "Effects of smoking upon sustained performance in a simulated driving task." Annals of the New York Academy of Sciences. (1967) 142:295-307.
- Henningfield, J.E. "Behavioral pharmacology of cigarette smoking." IN: Advances in Behavioral Pharmacology. T. Thompson, P.B. Dews, and J.E. Barrett (eds). Academic Press, New York. (1984) p 131-210.
- Hoffmann, D., Haley, N.J., Adams, J.D., and Brunemann, K.D. "Tobacco sidestream smoke: uptake by nonsmokers." Preventive Medicine. (1984) 13:608-617.
- Hull, C.L. The Influence of Tobacco Smoking on Mental and Motor Efficiency. Psychological Review Company, Princeton NJ. (1924) vol 33, p 1-161.
- Jarvis, M.J., Russell, M.A.H., and Feyerabend, C. "Absorption of nicotine and carbon monoxide from passive smoking under natural conditions of exposure." Thorax. (1983) 38:829-833.
- Knott, V.J. "Psychophysiological correlates of smokers and non-smokers: studies on cortical, autonomic and behavioural responsivity." IN: Electrophysiological Effects of Nicotine. A. Remond, and C. Izard (eds). Elsevier/North Holland Biomedical Press, Amsterdam. (1978a)
- Knott, V.J. "Smoking, EEG, and input regulation in smokers and non-smokers." IN: Smoking Behavior: Physiological and Psychological Influences. R.E. Thornton (eds). Churchill Livingston, New York. (1978b)
- Lippold, O.C., Williams, E.J., and Wilson, C.G. "Finger tremor and cigarette smoking." British Journal of Clinical Pharmacology. (1980) 10(1):83-86.
- Lippold, O.C.J., Williams, E.J., and Wilson, C.G. "Finger tremor and cigarette smoking." British Journal of Clinical Pharmacology. (1980) 10:83-86.

- Lyon, R., Tong, J.E., Leigh, G., and Claire, B. "The influence of ethanol and tobacco on the components of choice reaction-time." Journal of Studies on alcohol. (1975) 36:587-596.
- Mangan, B.L. "The effects of cigarette smoking on vigilance performance." Journal of General Psychology. (1982) 106:77-83.
- Muller, K.E., Barton, C.N., and Benignus, V.A. "Recommendations for appropriate statistical practice in toxicologic experiments." Neurotoxicology. (1984) 5(2):113-125.
- Myrsten, A.L., Post, B., Frankenhaeuser, M., and Johansson, G. "Changes in behavioral and physiological activation induced by cigarette smoking in habitual smokers." Psychopharmacologia (Berl). (1972) 27:305-312.
- Myrsten, A.L., Andersson, K., Frankenhaeuser, M., and Elgerot, A. "Immediate effects of cigarette smoking as related to different smoking habits." Perceptual and Motor Skills. (1975) 40:515-523.
- National Research Council. Environmental Tobacco Smoke. Measuring Exposures and Assessing Health Effects.. National Academy Press, Washington, DC. (1986)
- Shiffman, S.M., Gritz, E.R., Maltese, J., Lee, M.A., Schneider, N.B., and Jarvik, M.E. "Effects of cigarette smoking and oral nicotine on hand tremor." Clinical Pharmacology and Therapeutics. (1983) 33(6):800-805.
- Smith, D.L., Tong, J.E., and Leigh, G. "Combined effects of tobacco and caffeine on the components of choice reaction-time, heart rate, and hand steadiness." Perceptual and Motor Skills. (1977) 45:635-639.
- Tarriere, C., and Hartemann, F. "Investigation into the effects of tobacco smoke on a visual vigilance task." Proceedings of the 2nd International Congress of Ergonomics. (1964) 525-530.
- Thornton, R.E. Smoking Behavior: Physiological and Psychological Influences.. Churchill Livingstone, Edinburgh. (1978)
- Tong, J.E., Knott, V.J., McGraw, D.F., and Leigh, G. "Ethanol, visual discrimination and heart-rate: Effects of dosage, activation and tobacco." Quarterly Journal of Studies on Alcoholism. (1974) 35:1003-1022.
- Tong, J.E., Henderson, P.R., and Chippenfield, B.G.A. "Effects of ethanol and tobacco on auditory vigilance performance." Addictive Behaviors. (1980) 5:153-158.

- Wald, N.J., Idle, M., Boreham, J., and Bailey, A. "Carbon monoxide in breath in relation to smoking and carboxyhaemoglobin levels." Thorax. (1981) 36:366-369.
- Wald, N.J., Boreham, J., Bailey, A., Ritchie, C., Haddow, J.E., and Knight, G. "Urinary cotinine as marker for breathing other people's tobacco smoke." Lancet. (1984) 1:230-231.
- Warburton, D.M., and Wesnes, K. "Individual differences in smoking and attentional performance." IN: Smoking Behaviour. R.E. Thornton (eds). Churchill Livingstone, Edinburgh. (1978) p 19-43.
- Wesnes, K., Warburton, D.M., and Matz, B. "Effects of nicotine on stimulus sensitivity and response bias in a visual vigilance task." Neuropsychobiology. (1983) 9:41-44.
- Wesnes, K., and Warburton, D.M. "Effects of smoking on rapid information processing performance." Neuropsychobiology. (1983a) 9:223-229.
- Wesnes, K., and Warburton, D.M. "Smoking, nicotine and human performance." Pharmacological Therapeutics. (1983b) 21:189-208.
- Wesnes, K., and Warburton, D.M. "The effects of cigarettes of varying yield on rapid information processing performance." Psychopharmacology. (1984) 82:338-342.
- Williams, D.G. "Effects of cigarette smoking on immediate memory and performance in different kinds of smokers." British Journal of Psychology. (1980) 71:83-90.